Claims 1-4, 9-14 and 19 are pending. Applicants have hereinabove amended Claims 1, 9 and 19.. Therefore, claims 1-4, 9-14, and 19 are under examination. Support for amended Claims 1, 9 and 19 may be found *inter alia* the specification and specifically on page 2, lines 17-23; page 12, line 33 - page 13, line 22; and page 25, lines 3-25. Applicants respectfully submit that no new matter has been added. Accordingly, Applicants respectfully request the Examine to enter the Amendment.

Double Patenting Rejection

In the June 8, 1998 Office Action, the Examiner rejected Claim 19 under 35 U.S.C. 101 as claiming the same invention as that of Claim 1 of prior U.S. Patent No. 5,591,629. The Examiner asserted that this is a double patenting rejection.

In response, Applicant traverses the double patenting rejection of Claim 19 under 35 U.S.C. 101. Applicant will consider filing a Terminal Disclaimer upon an indication from the Examiner of allowable subject matter. Accordingly, Applicants respectfully request the Examiner to hold the rejection in abeyance until such time.

Rejection under 35 USC §102

In the June 8, 1998 Office Action, the Examiner maintained the rejection of Claims 1-4, 9, and 11-14 under 35 U.S.C. 102(b) as being anticipated by Miller et al (J. Neurosci., 14:6230-6238, 1994) for reasons made of record.

In response, Applicants traverse the Examiner's rejection of Claims 1-4, 9, and 11-14 under 35 U.S.C. §102 as being anticipated by Miller et al. Applicants maintain that Miller et al is not a proper reference and should be withdrawn.

Applicants maintain that the subject matter defined by the Claims is entitled to claim the benefit of U.S. Serial No. 08/236,520, filed April 29, 1994 (hereinafter the "'520 Application"), now U.S. Patent No. 5,591,629 (hereinafter the "'629 Patent"). The '520 Application provides an adequate written description of the subject matter now claimed in the instant invention. Claim 1 recites a method of stimulating remyelination of central nervous system axons in a mammal which comprises administering to said mammal an effective amount of an autoantibody selected from the group consisting of SCH 94.03, SCH 79.08, O1, O4, A2B5, HNK-1, antigen binding fragments thereof, and isolated or synthetic autoantibodies capable of inducing remyelination of central nervous system axons.

The '520 Application provides a written description for 1) SCH 94.03 (see Column 2, lines 1-11 of the '629 Patent); 2) O4, and A2B5 (see Column 8, lines 15 - 35; and of the '629 Patent); and 3) isolated or synthetic autoantibodies capable of inducing remyelination of central nervous system axons (see Column 9, lines 4-20; and Column 11, lines 1-34 of the '629 Patent). Also, in regard to O1, O4, A2B5, HNK-1, publications cited in the specification of the '629 Patent

describe O1, O4, A2B5, HNK-1. For example, Bansal, R., et al., "Stimulation of Oligodendrocyte Differentiation in Culture by Growth in the Presence of a Monoclonal Antibody to Sulfated Glycolipid," J. Neuro. Res. 21: 260-267 (1988) which note in particular, O4 as oligodendrocyte and specifically cites Sommer and Schachner, "Monoclonal antibodies (01 to 04) to oligodendrocyte cell surfaces: An immunocytological study in the central nervous system," Dev. Biol. 83: 311-327 (1981) and Schachner, "Cell type-specific surface antigens in the mammalian nervous system," J. Neurochem. 39:1-8 (1982), which describes four antibodies, designated 01, 02, 03, and 04 that react with the cell surfaces of oligodendroglia. These cited references are not included as exhibits attached hereto because they have already been submitted in connection with the instant application and were cited as part of the instant application. Lastly, Applicants respectfully submit that the O1, O4 and HNK-1 antibodies represent antibodies recognizing characteristic and cell type defining oligodendrocyte surface marker antigens as described and detailed in the '629 Patent.

Thus, Applicants are entitled to the benefit of the April 29, 1996 filing date of the parent application. Therefore, Miller et al. which was published after April 29, 1996 is not available for prior art purposes under 35 U.S.C. §102. Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the 35 U.S.C. §102 rejection of the claims.

Rejections under 35 U.S.C. § 112

In the June 8, 1998 Office Action, the Examiner rejected Claims 1-4, 9-14 and 19 under 35 U.S.C. § 112, first paragraph, because the Specification, while being enabling for methods of stimulating remyelination or treating a demyelinating disease in a mammal by administering to a mammal an effective amount of the monoclonal antibody A2B5, the Examiner asserted that the specification does not reasonably provide enablement for, isolated or synthetic autoantibodies or treatment of a demyelinating disease in mice or humans. The Examiner notes that Applicants assert that SCH94.03 and SCH79.08 have been deposited under the terms of the Budapest Treaty and thus all the requirements for deposit have been met, and submits the ATCC facsimile receipts to support deposit under the Budapest Treaty. However, the Examiner asserted that this showing is insufficient because: "If the deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by Applicant or Assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this Application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the Specification to recite the date of deposit and the complete name and full street address of the depository is required."

In response, Applicants respectfully traverse the Examiner rejection of claims 1-4, 9-14 and 19

under 35 U.S.C. §112, first paragraph. Applicants have hereinabove amended the specification to recite the deposit details. Further, Applicants attach hereto as Exhibits A and B, copies of the ATCC deposit certificates. Applicants hereby state that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this Application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. Therefore, Applicants are in compliance with all the terms and conditions of Budapest Treaty. Accordingly, Applicants respectfully requests that the examiner reconsider and withdraw the rejection of the Claims under 35 U.S.C. §112, first paragraph.

In addition, in the Office Action the Examiner rejected Claims 1-4, 9-14 and 19 under 35 U.S.C. § 112, first paragraph, because certain hybridomas and/or monoclonal antibodies are allegedly not freely commercially available to the public.

In response, Applicants respectfully traverse the Examiner rejection of claims 1-4, 9-14 and 19 under 35 U.S.C. §112, first paragraph. Applicants maintain that O1, and O4 were at the time of filing the subject application and continue to be publically available. Applicants are in the process of gathering such evidence and will forward it to the Examiner. Lastly, Applicants previously submitted a copy of the ATCC Catalogue of Cell lines and Hybridomas which demonstrated that HNK- I is publically available. However, for the convenience of the Examiner, Applicants attach hereto as Exhibit C the page from the ATCC Catalogue of Cell lines and Hybridomas. Accordingly, Applicants respectfully requests that the examiner reconsider and withdraw the rejection of the Claims under 35 U.S.C. §112, first paragraph.

In the June 8, 1998 Office Action, the Examiner asserted that the Specification does not provide support for isolate or synthetic autoantibodies having the characteristics thereof for the reasons set forth below. The Examiner asserted that the evidence does not support isolated polyclonal antibodies such as autoantibodies or synthetic autoantibodies.

In response, Applicants respectfully traverses the Examiner rejection of claims 1-4, 9-14 and 19 under 35 U.S.C. §112, first paragraph. Applicants maintain that the Specification provides an adequate written description to enable one skilled in the art to practice Applicants' invention (see Specification page 7, line 12 through to page 8, line 9 and page 11, lines 11 and 23). The Specification clearly provides one of skill in the art that "synthetic" autoantibody indicating an engineered or manipulated antibody or fragment thereof is in direct contrast to an "isolated" autoantibody or fragment thereof. Indeed as defined on page 11, line 6 of the Specification, natural or physiologic autoantibodies are present normally in serum. Thus, in contradistinction, "synthetic" autoantibodies, are those not normally present in serum. The Specification at pages 7-8 directs one of skill in the art to a series of references readily available to one of skill in the art, thereby teaching how to isolate the antibodies of the instant invention and how to generate the synthetic antibodies of the instant invention. Further, generation of polyclonal antibodies is generally a preliminary step in the production *of monoclonal* antibodies, the teaching of which

the Examiner now admits is enabled by the instant disclosure. More specifically, Applicants submit that the '629 Patent (column 7, line 59 through to column 8, line 8) teaches how to make and screen for such autoantibodies. Moreover, the issued patent well as the instant disclosure exemplify the generation of such autoantibodies using SJL/J mice. Applicant points out that both the issued patent and the instant Specification and incorporated references detail lists of both TMEV and EAE susceptible animal models. Because some animals are particularly susceptible to TMEV-induced demyelinative disease and others are demyelination refractive, it would be readily clear to one of skill in the art which animals to use in generating such autoantibodies. Therefore, the Specification provides an adequate written description to enable one skilled in the art to practice Applicants' invention. Accordingly, Applicants respectfully requests that the Examiner reconsider and withdraw the rejection under 35 U.S.C.§ 112, first paragraph.

In the June 8, 1998 Office Action, the Examiner rejected Claims 1-4, 9-14 and 19 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The Examiner stated that claims 1, 9 and 19 are unclear in the recitation of "isolated or synthetic autoantibodies having the characteristics thereof' because it is unclear as to what characteristics are required i.e. isotype, idiotype, IgG, IgM) by the autoantibody.

In response, Applicants have hereinabove amended the claims. Therefore, Claims 1-4, 9-14 and 19 are definite and particularly point out and distinctly claim the subject matter which Applicants' regard as the invention. Accordingly, Applicants respectfully requests that the Examiner reconsider and withdraw the rejection under 35 U.S.C.§ 112, second paragraph.

SUMMARY

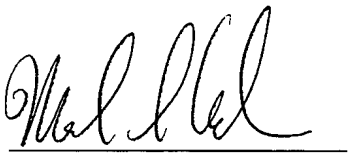
In view of the preceding Amendment and Remarks, Applicants contend that the subject matter defined by the claims is now in condition for allowance and earnestly solicit favorable action on all pending claims, namely Claims 1-4, 9 -14 and 19.

No fees are believed to be necessitated by the instant response. However, if any fee is required, authorization is hereby given to charge Deposit Account No. 11-1153 for any underpayment, or to credit any overpayments.

Early and favorable action on the claims is earnestly solicited.

Respectfully submitted,

KLAUBER & JACKSON



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